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This *Journal*, founded by the Medical Society for the Study of the Venereal Diseases, publishes original work on the investigation and treatment of genitourinary and allied disorders, and review articles, correspondence, and abstracts.

**Advice to authors** Papers for publication, which will be accepted on the understanding that they have not been and will not be published elsewhere and are subject to editorial revision, should be sent in duplicate to Dr A Mindel, Academic Department of Genitourinary Medicine, James Pringle House, Middlesex Hospital, London W1N 8AA. All authors must give signed consent to publication. The editor should be notified of any change of address of the corresponding author. Manuscripts will only be acknowledged if a stamped addressed postcard or international reply coupon is enclosed.

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(1) *Scripts (including correspondence and book reviews)* must be typewritten on one side of the paper in double spacing with ample margins. Two copies should be sent; if a paper is rejected, one copy will be retained.

(2) *Each script* should include, in the following order: a brief summary, typed on a separate sheet, outlining the main observations and conclusions; the text divided into appropriate sections; acknowledgements; references; tables, each on a separate sheet; and legends for illustrations.

(3) *The title* of the paper should be as brief as possible.

(4) *The number of authors* should be kept to the minimum, and only their initials and family names used.

(5) *Only the institution(s)* where work was done by each author should be stated.

(6) *SI units* are preferred. If old fashioned units are used, SI units should be given in parentheses or, for tables and figures, a conversion factor given as a footnote.

(7) *Only recognised abbreviations* should be used.

(8) *Acknowledgements* should be limited to workers whose courtesy or help extended beyond their paid work, and supporting organisations.

(9) *Figures* should be numbered in the order in which they are first mentioned, referred to in the text, and provided with captions typed on a separate sheet. (*Diagrams*: use thick, white paper and insert lettering lightly in pencil. *Photographs*: should be marked lightly on the back with the author's name and indicating the top, and should not be attached by paper clips or pins. They should be trimmed to include only the relevant section (sizes 2 1/4" or 5 1/4" wide, maximum 5 3/4" x 7") to eliminate the need for reduction. Photomicrographs must have internal scale markers. X ray films should be submitted as photographic prints, carefully prepared so that they bring out the exact point to be illustrated.

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legends to figures. Authors must take full responsibility for the accuracy of their references, and the list should be kept as short as practicable. It should be in the order in which references are first mentioned, and should include (in the following order), *journals*: author's name and initials, title of paper, name of journal (in full or abbreviated according to the list in *Index Medicus*), year of publication, volume number, and first and last page numbers; *books*: author's name and initials, full title, edition, place of publication, publisher, and year of publication. When a chapter in a book is referred to, the name and initials of the author of the chapter, title of the chapter, "In:", name and initials of the editor, and "ed" should precede book title, etc as above. In references to journals or books, when there are seven or more authors the names of the first three should be given followed by "et al." Names of journals no longer published should be given in full — for example, *British Journal of Venereal Diseases*.

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## Notices

### **International Union against the Venereal Diseases and Treponematoses (IUVDT)—sixth regional conference of the South East Asian and Western Pacific branch**

The sixth regional conference of the South East Asian and Western Pacific branch of the IUVDT will be held on 13–15 September 1989 in Darwin, Northern Territory, Australia, to talk about sexually transmissible diseases including AIDS.

For further information please contact IUVDT Darwin Conference, Communicable Diseases Centre, PO Box 41096, Casuarina, NT 5792, Australia.

### **International Union against Venereal Diseases and the Treponematoses (IUVDT)—35th general assembly**

The 35th general assembly of the IUVDT will be held on 9–11 May 1990 at the Royal Society of Medicine, London. The subject will be "Sexually transmitted diseases in the age of AIDS".

For further details please contact Barbara Komoniewska BA, Assistant Medical Services Secretary, Royal Society of Medicine, 1 Wimpole Street, London W1M

8AE (01 408 2119, telex 298902 ROYMED G).

### **Northern Genitourinary Physicians Colposcopy Group**

The increasing incidence of cervical intraepithelial neoplasia (CIN) and infection with human papillomavirus (the possible aetiological agent of CIN) in patients attending genitourinary medicine (GUM) clinics has led to colposcopy being used in many clinics. To discuss problems associated with providing a colposcopy service and to promote research into diagnosing and treating sexually transmitted disease of the cervix in relation to CIN and colposcopy, 18 GUM consultants from northern England (north of Birmingham and south of Scotland) inaugurated a colposcopy group on 12 November 1988, with Dr D A Hicks of the Royal Hallamshire Hospital, Sheffield, as president. Membership of the group is open to all colleagues in this geographical area.

Details of membership and the next meeting, to be held on 6 May 1989, are available from the honorary secretary, Dr A B Alawattagama, Academic Department of Genitourinary Medicine, Royal Liverpool Hospital, Prescott Street, Liverpool L7 8XP (051 709 0141).

### **International congress on viral infections as a cause of sexually transmitted diseases**

The Dutch Society for the Study of Sexually Transmitted Diseases is holding an international congress on "Viral infections as a cause of STD" in Amsterdam on 17 and 18 November 1989.

For further information please contact Hoboken Congress Organisation, Erasmus University Rotterdam, PO Box 1738, 3000 DR Rotterdam, The Netherlands.

### **Artificial Intelligence in Medicine—call for papers**

The next two volumes of the new international quarterly journal, *Artificial Intelligence in Medicine*, vol 2 (1990) and vol 3 (1991), will be devoted to studies in medical knowledge engineering. Papers on all aspects of medical expert systems, including their designing, application and evaluation, are welcome. Contributions should be sent to the editor: Professor KS Zadeh, University of Münster Hospital, Department of Medical Informatics, Münster, West Germany 4400.

Electronic manuscripts are preferred. Details and instructions for authors may be obtained from the publisher: Burgverlag, PO Box 1247, Tecklenburg, West Germany 4542.

# List of current publications

*Selected abstracts and titles from recent reports published worldwide are arranged in the following sections:*

*Syphilis and other treponematoses*

*Gonorrhoea*

*Non-specific genital infection and related disorders*

(*chlamydial infections; mycoplasmal and ureaplasma infections; general*)

*Pelvic inflammatory disease*

*Reiter's disease*

*Trichomoniasis*

*Candidiasis*

*Genital herpes*

*Genital warts*

*Acquired immune deficiency syndrome*

*Other sexually transmitted diseases*

*Genitourinary bacteriology*

*Public health and social aspects*

*Miscellaneous*

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## *Syphilis and other treponematoses*

**Identification, cloning and purification of protein antigens of *Treponema pallidum***

LV STAMM, WS DALLAS, PH RAY, PJ BASSFORD Jr (Chapel Hill, USA). *Rev Infect Dis* 1988;10suppl:403-7.

**Early syphilitic hepatitis after renal transplantation**

PC JOHNSON, SJ NORRIS, GPG MILLER, *et al* (Houston, USA). *J Infect Dis* 1988;158:236-7.

**Ocular syphilis in patients with human immunodeficiency virus infection**

MS PASSO, JJ ROSENBAUM (Portland, USA). *Am J Ophthalmol* 1988;106:1-6.

Although recent published reports abound with examples of ocular manifestations of the acquired immune deficiency syndrome, cases of ocular syphilis in patients infected with human immunodeficiency virus (HIV) are described relatively rarely. In this paper the authors present case reports of three homosexual men infected with HIV whose eyes were affected by syphilis. The first was a man aged 42 who had uveitis of the left eye. Five months earlier he had developed malaise, lymphadenopathy, and a macular rash on his forearms and trunk. Biopsy of adenoidal tissue showed granulomatous inflammation, a tentative diagnosis of Wegener's granulomatosis was made, and oral treatment with prednisolone was started. Three weeks later the uveitis worsened, becoming bilateral. An infectious disease

consultant obtained a history of contact with male prostitutes and noted a maculopapular rash on the trunk, palms, and soles. Serology gave positive results in the rapid plasma reagin (RPR) test at a titre of 1/128 and the fluorescent treponemal antibody absorption (FTA-ABS) test. An HIV antibody test gave positive results by enzyme linked immunosorbent assay (ELISA) and western blot. Examination of the cerebrospinal fluid (CSF) showed a high protein concentration, a high cell count, and a positive reaction in the FTA-ABS test. Secondary syphilis was diagnosed, and because the patient was allergic to penicillin he was given chloramphenicol 2 g a day for 14 days. During the subsequent four weeks the uveitis resolved, although recovery was complicated by a retinal detachment that required scleral buckling.

Case two was a man aged 38 who developed malaise and lymphadenopathy. Four months later he developed a rash on his elbow, which varied in severity during the following nine months and at times affected his palms and soles. Results of the Venereal Diseases Research Laboratory (VDRL) and HIV antibody tests were negative, and the rash was diagnosed as psoriasis. Several months later he returned complaining of headache, weight loss, and blurred vision. His HIV antibody test result was now positive, and AIDS related complex was diagnosed. Two months later, ocular examination showed evidence of uveitis. Visual acuity improved after a three month course of local corticosteroids and cycloplegics. It was not until after another seven months that a systemic cause for the

uveitis was sought. Laboratory results showed a positive VDRL test result at a titre of 1/256 and a positive FTA-ABS test result, and CSF examination showed evidence of active neurosyphilis. He was treated intravenously with 2.4 MIU penicillin G every four hours for 10 days, followed by 2.4 MIU benzathine penicillin a week for three weeks, which resulted in rapid resolution of the rash and uveitis. The uveitis recurred a few months later, but he had no evidence of recurrent syphilis, and the uveitis responded to topical prednisolone. When he was last seen there was no evidence of active uveitis.

The third case was in a bisexual man aged 27 with a history of intravenous drug abuse, who was referred for evaluation of uveitis. He claimed to have had a negative HIV antibody test result six months before. General examination showed diffuse lymphadenopathy and an erythematous maculopapular rash on his palms and soles, which had been ascribed to a longstanding fungal infection. Ophthalmic examination showed uveitis affecting predominantly the left eye, and treatment with topical corticosteroids and cycloplegics was begun. Serology showed a positive VDRL test result at a titre of 1/64 and a positive FTA-ABS test result, CSF examination showed evidence of neurosyphilis, and the HIV antibody test was positive by ELISA and western blot analysis. The patient was treated with penicillin in exactly the same way as in case 2. He was seen in an emergency department one year later complaining of bilateral floaters, but ophthalmic examination showed no appreciable abnormal-

mality, and CSF examination showed no evidence of active syphilis. He was lost to follow up.

In each case the diagnosis of syphilis was not initially suspected, and in fact the first patient had consulted 10 doctors (including seven specialists) before the diagnosis was established. This perhaps highlights a low level of suspicion of sexually transmitted infection in doctors not specialising in genitourinary medicine. The authors suggested several factors that may have contributed to the delay in making the correct diagnosis. Among these were (1) that HIV infection may alter the serological response to syphilis, as in case 2 where the patient had a negative VDRL result despite an active rash; (2) that a diagnosis of HIV infection may have dissuaded physicians from looking for a treatable cause of uveitis; and (3) that spontaneous improvement after treatment with corticosteroids may have suggested that the ocular disease was non-infectious in origin.

The authors also discussed how the coexistence of HIV infection and syphilis may alter the diagnosis and response to treatment and suggested that, as the incidence of ocular complications and neurosyphilis may be increased in the presence of HIV infection, all patients with syphilis should be tested for antibodies to HIV and vice versa. Furthermore, they recommended that the CSF should be examined to exclude neurosyphilis if the patient is HIV positive or has secondary syphilis.

J Forrer

#### **Lues maligna in a patient with human immunodeficiency virus infection**

D SHULKIN, L TRIPOLI, E ABELL (Pittsburgh, USA). *Am J Med* 1988;85:425-7.

#### **Syphilitic polyradiculopathy in an HIV positive man**

MJ LANSKA, DK LANSKA, JW SCHMIDLEY (Cleveland, USA). *Neurology* 1988;38:1297-301.

### **Gonorrhoea**

#### **Lipooligosaccharides: the principal glycolipids of the neisserial outer membrane**

JM GRIFFISS, H SCHNEIDER, RE MANDRELL, *et al* (San Francisco, USA). *Rev Infect Dis* 1988;10suppl:287-95.

#### **Understanding the structure and antigenicity of gonococcal pili**

ED GETZOFF, HE PARGE, DE MCREE, JA TAINER

(La Jolla, USA). *Rev Infect Dis* 1988;10suppl:296-9.

#### **Surveillance of the antibiotic susceptibility of non-penicillinase producing *Neisseria gonorrhoeae* in the Netherlands from 1983 to 1986**

B VAN KLINGEREN, MC ANSINK-SCHIPPER, L DOORNBOS, *et al* (Bilthoven, Netherlands). *J Antimicrob Chemother* 1988;21:737-44.

#### **Single-dose cefotaxime intramuscularly cures gonococcal ophthalmia neonatorum**

P LEPAGE, J BOGAERTS, P KESTELYN, A MEHEUS (Kigali, Rwanda). *Br J Ophthalmol* 1988;72:518-20.

### **Non-specific genital infection and related disorders (chlamydial infection)**

#### **Antigenic structure of surface-exposed regions of the major outer-membrane protein of *Chlamydia trachomatis***

WJ NEWHALL (Indianapolis, USA). *Rev Infect Dis* 1988;10suppl:386-90.

#### **Staining characteristics of six commercially available monoclonal immunofluorescence reagents for direct diagnosis of *Chlamydia trachomatis* infections**

LD CLES, K BRUCH, WE STAMM (Seattle, USA). *J Clin Microbiol* 1988;26:1735-7.

#### **Sensitive immune dot blot test for diagnosis of *Chlamydia trachomatis* infection**

G MEARN, SJ RICHMOND, CC STOREY (Manchester, England). *J Clin Microbiol* 1988;26:1810-3.

#### ***Chlamydia trachomatis* Fitz-Hugh-Curtis syndrome without salpingitis in female adolescents**

DK KATZMAN, IM FRIEDMAN, CA McDONALD, IF LITT (Stanford, USA). *Am J Dis Child* 1988;142:996-8.

#### **Susceptibility testing of *Chlamydia trachomatis*: from eggs to monoclonal antibodies**

JM EHRET, FN JUDSON (Denver, USA). *Antimicrob Agents Chemother* 1988;32:1295-9.

#### **Activity of spiramycin against chlamydia, *in vitro* and *in vivo***

J ORFILA, F HAIDER, D THOMAS (Amiens, France). *J Antimicrob Chemother* 1988;22:73-6.

### **Non-specific genital infection and related disorders (mycoplasmal and ureaplasma infections)**

#### **Protein antigens of genital mycoplasmas**

GH CASSELL, HL WATSON, DK BLALOCK, SA HOROWITZ, LB DUFFY (Birmingham, USA). *Rev Infect Dis* 1988;10suppl:391-8.

### **Non-specific genital infection and related disorders (general)**

#### **The efficacy and safety of spiramycin in the treatment of non-gonococcal urethritis in men**

S SEGEV, Z SAMRA, E ELIAV, N ROSEN, E RUBINSTEIN (Hashomer, Israel). *J Antimicrob Chemother* 1988;22:183-8.

### **Pelvic inflammatory disease**

#### **Etiology and outcome of acute pelvic inflammatory disease**

RC BRUNHAM, B BINNS, F GUIJON, *et al* (Manitoba, Canada). *J Infect Dis* 1988;158:510-7.

### **Reiter's syndrome**

#### **Seronegative (reactive) arthropathy: precipitating factors**

EDITORIAL. *Lancet* 1988;ii:200-1.

#### **Light and electron microscopic studies on the synovial membrane in Reiter's syndrome—immunocytochemical identification of chlamydial antigen in patients with early disease**

HR SCHUMACHER, S MAGGE, PV CHERIAN, *et al* (Philadelphia, USA). *Arthritis Rheum* 1988;31:937-46.

Schumacher *et al* describe the histological features of synovial biopsy specimens from 15 male patients with Reiter's syndrome. Needle biopsy was performed in 14 and open biopsy in one who was undergoing synovectomy for Achilles tenosynovitis.

The time between the onset of the episode of arthropathy and biopsy ranged from under four weeks to four months, and the time from the first episode of Reiter's syndrome to biopsy ranged from under one month to 24 years. Synovial tissue obtained

was fixed for light microscopy and for transmission electron microscopy.

All patients had at least one sample of fluid aspirated from the affected joint. The synovial fluid leucocyte count ranged from  $4.75 \times 10^6/l$  to  $59 \times 10^6/l$ , with a predominance of neutrophils in all but one patient. In three patients the "Reiter's cell" (a macrophage with a phagocytised nucleus) was seen. Routine bacterial cultures of the aspirated fluid gave negative results. Samples of synovial fluid were also found to be free from crystals.

Studies by light microscopy of synovium obtained from 11 patients during the first month of an episode showed proliferation of synovial lining cells, increased surface fibrin, and vascular congestion. Biopsy specimens taken later in the course of the episode showed similar features but a tendency towards increased infiltration with lymphocytes and plasma cells.

Electron microscopy of samples from eight patients during the first months after a diagnosis of Reiter's syndrome showed occlusion of vessels by platelets in four, and fibrin or dense granular material in the vessel walls of four. Five of the patients had unidentified intracellular and extracellular particles; some of these were highly suggestive of chlamydiae. No such particles were noted in samples from three patients with more chronic disease.

This study provides an interesting histological description of the synovium in patients diagnosed as suffering from Reiter's syndrome. The demographic characteristics of the 15 patients studied, however, were confusing and inadequate. We are told that eight suffered from urethritis, but not whether this was present at the time of synovial biopsy or was one of the features from which Reiter's syndrome had been diagnosed, nor are we informed whether urethral cultures for chlamydiae were taken. A basic lack of understanding of these important questions is apparent in the fact that only three of the patients with urethritis received antibiotic treatment; one with intravenous penicillin and the other two with tetracycline.

P D Woolley

## Trichomoniasis

### The effect of hormones on *Trichomonas vaginalis*

B SUGARMAN, N MUMMAW (Michigan, USA). *J Gen Microbiol* 1988;134:1623-8.

### New rapid latex agglutination test for diagnosing *Trichomonas vaginalis* infection

JA CARNEY, P UNADKAT, A YULE, R RAJAK-UMAR, C JN LACEY, JP ACKERS (Guildford, England). *J Clin Pathol* 1988;41:806-8.

### Monoclonal-antibody-based enzyme-linked immunosorbent assay for *Trichomonas vaginalis*

H MAUCH, W BREHMER, HH SONNEBORN, J HORN, S WAGNER (Berlin, Federal Republic of Germany). *J Clin Microbiol* 1988;26:1684-6.

## Candidiasis

### Interaction of *Candida albicans* with genital mucosa: effect of sex hormones on adherence of yeasts *in vitro*

A KALO, E SEGAL (Tel Aviv, Israel). *Can J Microbiol* 1988;34:224-8.

### Single dose therapy of vulvovaginal candidosis: comparison of terconazole and clotrimazole

E VARTIAINEN, O WIDHOLM (Helsinki, Finland). *Curr Ther Res* 1988;44:185-8.

### Treatment of vaginal candidiasis with a single oral dose of fluconazole

MULTICENTRE STUDY GROUP. *Eur J Clin Microbiol Infect Dis* 1988;7:364-7.

### Azole antifungal drugs: old and new

WE DISMUKES (Birmingham, USA). *Ann Intern Med* 1988;109:177-8.

## Genital herpes

### Comparison of diploid fibroblast and rabbit tissue cultures and a diploid fibroblast microtitre plate system for the isolation of herpes simplex virus

A LANGENBERG, R ZBANYSEK, J ORAGAVON, R ASHLEY, L COREY (Seattle, USA). *J Clin Microbiol* 1988;26:1772-4.

### Virological screening for herpes simplex virus during pregnancy

EDITORIAL. *Lancet* 1988;ii:722-3.

### Changing presentation of herpes simplex virus infection in neonates

RJ WHITLEY, L COREY, A ARVIN, *et al* (Birmingham, USA). *J Infect Dis* 1988;158:109-16.

During studies of antiviral treatment for neonatal herpes simplex virus (HSV) infections, the authors observed a change in the pattern of presenting features in their

patients. This report compares the features of 95 neonates and their mothers seen in 1973-81 (the first period) with 196 seen in 1982-7 (the second period).

There were three categories of neonatal HSV infection: (1) disseminated, usually involving several organs; (2) central nervous system (CNS) (encephalitis); and (3) skin, eye, and mucous membrane (SEM). All cases occurred in babies under one month old and were virologically confirmed. The proportion of babies with SEM disease rose from 17.9% to 43.4% and of those with disseminated infections fell from 50.5% to 22.9% between the study periods. Babies in the second study period were more often white, less often premature, and had had signs of HSV infection for less time prior to study entry. The maternal characteristics, including age, parity, history of prior HSV, labour and delivery findings, did not differ between the two study periods, except that more were married in the second period. No significant differences were seen in HSV serology results between the study periods. The authors conclude that infants with HSV infections were being identified earlier, which was the main reason for the lower proportions of CNS and disseminated disease.

The report also provided additional evidence that most neonatal HSV infections occurred despite there being no history or clinical evidence of active HSV in the mother at the time of delivery. About a quarter of the mothers had a fever at delivery, however, which may be a useful clinical indicator. It was noted that caesarean section did not always prevent HSV infection, even when there was no prior rupture of membranes.

R Gilson

### Intravenous acyclovir therapy of first episodes of genital herpes—a multicenter double-blind, placebo-controlled trial

JE PEACOCK, *et al* (Salem, USA). *Am J Med* 1988;85:301-6.

### Long-term acyclovir suppression of frequently recurring genital herpes simplex virus infection

GJ MERTZ, CC JONES, J MILLS, *et al* (Albuquerque, USA). *JAMA* 1988;260:201-6.

## Genital warts

### The biology and significance of human papillomavirus infections in the genital tract

R REID, M CAMPION (Atlanta, USA). *Yale J Biol Med* 1988;61:307-26.

**Transformation of primary human fibroblast cells with human papillomavirus type 16 DNA and EJ-ras**

G MATLASHEWSKI, K OSBORN, L BANKS, M STANLEY, L CRAWFORD (Quebec, Canada). *Int J Cancer* 1988;42:232-8.

**Characterization of normal human exocervical epithelial cells immortalized in vitro by papillomavirus type-16 and type-18 DNA**

CP WOOLWORTH, PE BOWDEN, J DONIGER, *et al* (Bethesda, USA). *Cancer Res* 1988;48:4620-8.

**Synthetic oligonucleotide probes for the detection of human papillomaviruses by in situ hybridisation**

HA CUBIE, M NORVAL (Edinburgh, Scotland). *J Virol Methods* 1988;20:239-50.

**Correlation of cytologic, colposcopic and histologic studies with immunohistochemical studies of human papillomavirus structural antigens in an unselected patient population**

RW WAECKERLIN, NJ POTTER, GR CHEATHAM JR (Casper, USA). *Am J Obstet Gynecol* 1988;158:1394-401.

**Analysis of individual human papillomavirus types in cervical neoplasia: a possible role for type 18 in rapid progression**

RJ JURMAN, MH SCHIFFMAN, WD LANCASTER, *et al* (Washington, USA). *Am J Obstet Gynecol* 1988;159:293-8.

The aim of this study was to assess whether individual papillomavirus types were differentially detected in various grades of cervical intraepithelial neoplasia (CIN) and invasive squamous neoplasia. A correlated histopathologic and molecular approach was used in which individual types of HPV, specifically types 16 and 18, were analysed separately and compared. Two hundred and fourteen colposcopically directed cervical biopsy samples were obtained from women referred because of an abnormal cervical cytological smear to two clinics in the United States (Washington and Detroit) and one in Brazil (San Paulo). Half of each biopsy specimen was processed for conventional light microscopy; the other half was frozen and stored for molecular analysis by Southern blot hybridisation. About every fifteenth section was stained with haematoxylin and eosin and examined microscopically to confirm that the tissue sample studied by DNA hybridisation was comparable with the portion of the permanent specimen analysed by light microscopy.

Biopsy specimens obtained from the three clinics were analysed by DNA hybridisation,

and each result was compared with the histological diagnosis from the same tissue sample. Significant correlations were seen between HPV type and histological grade comparing all grades of CIN with invasive cancer ( $p < 0.001$ ). Of particular interest was the finding of HPV type 18 in only 3% of patients with CIN compared with 22% of those with invasive carcinoma ( $p < 0.001$ ). In contrast, no significant difference was seen in the incidence of HPV type 16 in CIN (37%) compared with invasive cancer (41%). These findings may represent a rapid transit time through the precursor stage for HPV type 18, which may play a part in the development of rapidly progressive cervical cancer.

The authors state that their results must be interpreted with caution because data regarding other potential risk factors, such as age, sexual history, parity, socioeconomic status, and race, were not available for all patients.

P D Woolley

**Immunohistochemistry (S100, KL1) and human papillomavirus DNA hybridization on Morbus Bowen and bowenoid papulosis**

A HAHN, T LÖNING, A HOOS, P HENKE (Hamburg, Federal Republic of Germany). *Virchows Arch [A]* 1988;413:113-22.

**Human papillomavirus and cancer of the uterine cervix**

TA BONFIGLIO, MH STOLER (Rochester, USA). *Hum Pathol* 1988;19:621-2.

**Human papillomaviruses and cervical cancer: analysis of histopathologic features associated with different viral types**

SP WILCZYNSKI, S BERGEN, J WALKER, S-Y LIAO, LF PEARLMAN (Irvine, USA). *Hum Pathol* 1988;19:697-704.

**Sexually transmitted diseases including genital papillomavirus infection in male sexual partners of women treated for cervical intraepithelial neoplasia III by conization**

P BISTOLETTI, P LIDBRINK (Huddinge, Sweden). *Br J Obstet Gynaecol* 1988;95:611-3.

**Human papillomavirus: untreated male reservoir**

PM KATELARI, YE COSSART, BR ROSE, *et al* (Darlinghurst, Australia). *J Urol* 1988;140:300-5.

**Prospects for human papillomavirus vaccines and immunotherapies**

AA SCHREIER, WP ALLEN, C LAUGHLIN, J

GRUBER (Bethesda, USA). *J Natl Cancer Inst* 1988;80:896-9.

**Genital condylomas in pregnancy: use of trichloroacetic acid and laser therapy**

DB SCHWARTZ, MD GREENBERG, Y DAOUD, R REID (Detroit, USA). *Am J Obstet Gynecol* 1988;158:1407-16.

**Acquired immune deficiency syndrome**

**AIDS—1987 revision of CDC/WHO case definition**

*Bull WHO* 1988;66:259-62.

**Regulation of HIV and HTLV gene expression**

H VARMUS (San Francisco, USA). *Genes Dev* 1988;2:1055-62.

**A novel gene of HIV-1, *vpu*, and its 16-kilodalton product**

K STREBEL, T KLIMKAIT, MA MARTIN (Bethesda, USA). *Science* 1988;241:1221-2.

**Nef protein of HIV-1 is a transcriptional repressor of HIV-1 LTR**

N AHMAD, S VENKATESAN (Bethesda, USA). *Science* 1988;241:1481-5.

**Isolation and characterisation of a novel protein (X-ORF product) from SIV and HIV-2**

LE HENDERSON, RC SOWDER, TD COPELAND, RE BENVENISTE, S OROSZLAN (Frederick, USA). *Science* 1988;241:199-201.

**Genetic variability between isolates of human immunodeficiency virus (HIV) type 2 is comparable to the variability among HIV type 1**

JF ZAGURY, G FRANCHINI, M REITZ, *et al* (Bethesda, USA). *Proc Natl Acad Sci USA* 1988;85:5941-5.

**Analysis of host-virus interaction in AIDS with anti-gp120 T cell clones: effect of HIV sequence variation and a mechanism for CD4+ cell depletion**

RF SILICIANO, T LAWTON, C KNALL, *et al* (Boston, USA). *Cell* 1988;54:561-75.

**Spontaneous cytotoxicity and tumour necrosis factor production by peripheral blood monocytes from AIDS patients**

SC WRIGHT, A JEWETT, R MITSUYASU, B BON-AVIDA (Redwood City, USA). *J Immunol* 1988;141:99-104.

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**Elevated levels of circulating cachectin/tumour necrosis factor in patients with acquired immunodeficiency syndrome**

J LAHDEVIRTA, CPJ MAURMY, AM TEPPÖ, H REPO (Helsinki, Finland). *Am J Med* 1988;**85**:289-91.

**Presence of antibodies to a putatively immunosuppressive part of human immunodeficiency virus (HIV) envelope glycoprotein gp41 is strongly associated with health among HIV-positive subjects**

PJ KLASSE, R PIPKORN, J BLOMBERG (Lund, Sweden). *Proc Natl Acad Sci USA* 1988;**85**:5225-9.

**Serum HIV antigen and anti-p24-antibodies in 200 seropositive patients: correlation with CD4 and CD8 lymphocyte subsets**

J-M ANDRIEU, D EME, A VENET, *et al* (Paris, France). *Clin Exp Immunol* 1988;**73**:1-5.

**Numbers of CD4+ cells and the levels of core antigens of and antibodies to the human immunodeficiency virus as predictors of AIDS among seropositive homosexual men**

F DE WOLF, JMA LANGE, JTM HOUWELING, *et al* (Amsterdam, Netherlands). *J Infect Dis* 1988;**158**:615-22.

**Candida and AIDS: evidence for protective antibody**

R MATTHEWS, J BURNIE, D SMITH, *et al* (London, England). *Lancet* 1988;ii:263-5.

**Live virus vaccines in human immunodeficiency virus-infected children—a retrospective survey**

M McLAUGHLIN, P THOMAS, J ONORATO, *et al* (New York, USA). *Pediatrics* 1988;**82**:229-33.

**Measurement of antibodies to human immunodeficiency virus—an international collaborative study to evaluate WHO reference sera**

AJ GARRETT, V SEAGROATT, EM SPURAN, KD HABERMEHL, H HAMPL, GC SCHILD (Potters Bar, England). *Bull WHO* 1988;**66**:197-202.

**Rapid latex agglutination assay using recombinant envelope polypeptide for the detection of antibody to HIV**

TC QUINN, CH RIGGIN, RL KLINE, *et al* (Bethesda, USA). *JAMA* 1988;**260**:510-3.

**Serological diagnosis of human immunodeficiency virus infection by Western blot testing**

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**Identification of HIV-infected seronegative individuals by a direct diagnostic test based on hybridisation to amplified viral DNA**

M LOCHE, B MACH (Geneva, Switzerland). *Lancet* 1988;ii:418-20.

**Detection of HIV-1 DNA in infants and children by means of the polymerase chain reaction**

F LAURE, V COURGNAUD, C ROUZIOUX, *et al* (Paris, France). *Lancet* 1988;ii:538-40.

**Direct detection of HIV RNA expression in seropositive subjects**

C HART, G SCHOCHETMAN, T SPIRA (Atlanta, USA). *Lancet* 1988;ii:596-8.

**A prospective study of HIV-2 prevalence in France**

A-M COUROUCE, AND THE RETROVIRUS STUDY GROUP OF THE FRENCH SOCIETY OF BLOOD TRANSFUSION (Paris, France). *AIDS* 1988;**2**:261-6.

**Trial of anonymous versus confidential human immunodeficiency virus testing**

LJ FEHRS, D FLEMING, LR FOSTER, *et al* (Santa Fe, USA). *Lancet* 1988;ii:379-81.

**Comparison of HIV-antibody prevalence in patients consenting to and declining HIV-antibody testing in an STD clinic**

HF HULL, CJ BETTINGER, MM GALLAHER, NM KELLER, J WILSON, GJ MERTZ (Santa Fe, USA). *JAMA* 1988;**260**:935-8.

**Human immunodeficiency virus infection among men with sexually transmitted diseases: experience from a center in Africa**

JN SIMONSEN, DW CAMERON, MN GAKINYA, *et al* (Cleveland, USA). *N Engl J Med* 1988;**319**:274-7.

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WE STAMM, HH HANDSFIELD, AM ROMPALO, RL ASHLEY, PL ROBERTS, L COREY (Seattle, USA). *JAMA* 1988;**260**:1429-33.

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**Frequency of nosocomial transmission of HIV infection among health care workers**

GP WORMSER, CS RABKIN, C JOLLINE (New York, USA). *N Engl J Med* 1988;**319**:307-8.

**HIV infection, breast feeding, and human milk banking**

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**AIDS: predicting cases nationally and locally**

BR TENNISON, S HAGARD (Cambridge, England). *Br Med J* 1988;**297**:711-2.

**Occult AIDS: Pneumocystis carinii pneumonia in elderly people**

MR HARGREAVES, GN FULLER, BG GAZZARD (London, England). *Br Med J* 1988;**297**:721-2.

**Pneumocystis carinii pneumonia: detection of parasites in sputum and bronchoalveolar lavage fluid by monoclonal antibodies**

KM ELVIN, A BJÖRKMAN, E LINDER, N HEURLIN, A HJERPE (Stockholm, Sweden). *Br Med J* 1988;**297**:381-3.

**Pneumocystis carinii antigenaemia in acquired immunodeficiency syndrome**

LW PIFER, BL WOLF, JJ WEEMS JR, DR WOODS, CC EDWARDS, RE JOYNER (Memphis, USA). *J Clin Microbiol* 1988;**22**:1357-61.

**Granulomatous pneumocystis-carinii pneumonia in 3 patients with the acquired immunodeficiency syndrome**

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**Trimethoprim-sulfamethoxazole compared with pentamidine for treatment of Pneumocystis carinii pneumonia in the acquired immunodeficiency syndrome: a prospective noncrossover study**

FR SATTTLER, R COWAN, DM NIELSEN, J RUSKIN (Los Angeles, USA). *Ann Intern Med* 1988;**109**:280-7.

**Survival and prognostic factors in severe pneumocystis-carinii pneumonia requiring mechanical ventilation**

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**Pneumocystis carinii otitis media and mastoiditis as the initial manifestation of the acquired immunodeficiency syndrome**

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**Retinal and gastrointestinal disease due to cytomegalovirus in patients with the acquired immune deficiency syndrome—prevalence, natural history and response to ganciclovir therapy**

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**Intravenous and intraocular ganciclovir for CMV retinitis in patients with AIDS or chemotherapeutic immunosuppression**

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**Randomized prospective trial of ganciclovir maintenance therapy for cytomegalovirus retinitis**

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**Immunomorphological analysis of the role of blood vessel endothelium in the morphogenesis of cutaneous Kaposi's sarcoma: a study of 57 cases**

F FACCHETTI, L LUCINI, R GAVAZZONI, F CALLEA (Brescia, Italy). *Histopathology* 1988;12:581–94.

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**Thrombotic thrombocytopenic purpura associated with human immunodeficiency virus type-1 (HIV-1) infection**

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**Thrombotic thrombocytopenic purpura in patients with the acquired immunodeficiency syndrome (AIDS)-related complex: a report of two cases**

JMG NAIR, R BELLEVUE, M BERTONI, H DOSIK

(New York, USA). *Ann Intern Med* 1988;109:209–12.

**Haematological abnormalities in human immunodeficiency virus (HIV) disease**

C COSTELLO (London, England). *J Clin Pathol* 1988;41:711–5.

**Benign lymphoepithelial parotid cysts and hyperplastic cervical adenopathy in AIDS-risk patients—a new CT appearance**

RA HOLLIDAY, WA COHEN, RA SCHINELLA, et al (New York, USA). *Radiology* 1988;168:439–42.

**Odynophagia from aphthous ulcers of the pharynx and oesophagus in the acquired immunodeficiency syndrome (AIDS)**

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**Acyclovir-resistant herpes in AIDS treated with foscarnet**

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**Progressive disseminated histoplasmosis in patients with acquired immunodeficiency syndrome**

PC JOHNSON, N KHANDORI, AF NAJJAR, F BUTT, PWA MANSELL, GA SARDESI (Dallas, USA). *Am J Med* 1988;85:152–8.

**Quantitative pathology of coccidiomycosis in acquired immunodeficiency syndrome**

AR GRAHAM, RE SABONYA, DA BRONNIMAN, JN GALGANI (Tuscon, USA). *Hum Pathol* 1988;19:800–6.

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MA JACOBSON, H GELLERMAN, H CHAMBERS (San Francisco, USA). *Am J Med* 1988;85:172–6.

**Increased risk of bacterial pneumonia in HIV-infected intravenous drug users without AIDS**

PA SELWYN, AR FEINGOLD, D ARTEL, et al (New York, USA). *AIDS* 1988;2:267–72.

**Infectious diarrhoea in patients with AIDS**

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**CNS Complications of AIDS—CT and MR findings**

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**Chronic progressive varicella-zoster virus encephalitis in an AIDS patient**

DH GILDEN, RS MURRAY, M WELLISH, BK KLEINSCHMIDTDEMASTERS, A VAFI (Denver, USA). *Neurology* 1988;38:1150–2.

**Prolonged survival and partial recovery in AIDS associated progressive multifocal leukoencephalopathy**

JR BERGER, L MUCKE (Miami, USA). *Neurology* 1988;38:1060–4.

**Cotton-wool spots in acquired immunodeficiency syndrome compared with diabetes mellitus, systemic hypertension, and central retinal vein occlusion**

AM MANSOUR, LM JAMPOL, S LOGANI, JS READ, D HENDERLY (Chicago, USA). *Arch Ophthalmol* 1988;106:1074–7.

**Human immunodeficiency virus-associated myopathy: analysis of 11 patients**

DM SIMPSON, AN BENDER (New York, USA). *Ann Neurol* 1988;24:79–84.



**Outcome of patients with human immunodeficiency virus on maintenance haemodialysis**

C ORTIZ, R MENESES, D JAFFE, JA FERNANDEZ, G PEREZ, JJ BOURGOIGNE (Miami, USA). *Kidney Int* 1988;34:248-53.

**Resolution of cytomegalovirus retinitis with zidovudine therapy**

DJ D'AMICO, PR SKOLNIK, BR KOSLOFF, P PINKSTON, MS HIRSCH, RT SCHOOLEY (Boston, USA). *Arch Ophthalmol* 1988;106:1168-70.

**Zidovudine overdosage**

JB SPEAR, HA KESSLER, SN LEHRMAN, P DE MIRANDA (Chicago, USA). *Ann Intern Med* 1988;109:76.

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**Effect of lithium carbonate on zidovudine-associated neutropenia in the acquired immunodeficiency syndrome**

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**Uridine reverses the toxicity of 3'-azido-3'-deoxythymidine in normal human granulocyte-macrophage progenitor cells in vitro without impairment of antiretroviral activity**  
J-P SOMMADOSSI, R CARLISLE, RF SCHINAZI, Z ZHOU (Birmingham, USA). *Antimicrob Agents Chemother* 1988;32:997-1001.

**Comparison of antigen immunoassay and reverse transcriptase assay for monitoring human immunodeficiency virus infection in an antiviral trial**

H BURGER, D APUL, FP SIEGAL, *et al* (Stony Brook, USA). *J Clin Microbiol* 1988;26:1890-2.

**Randomised, double-blind, placebo-controlled trial of ditiocarb sodium ("Imuthiol") in human immunodeficiency virus infection**

JM LANG, J-L TOURAINE, C TREPO, *et al* (Lyon, France). *Lancet* 1988;ii:702-5.

**Immunoglobulin preparations for HIV-infected patients**

PL YAP, PE WILLIAMS (Edinburgh, Scotland). *Vox Sang* 1988;55:65-74.

**Passive immunoneutralisation of human immunodeficiency virus in patients with advanced AIDS**

GG JACKSON, JT PERKINS, M RUBENIS, *et al* (London, England). *Lancet* 1988;ii:647-51.

**Regular review: prospects for vaccines against HIV**

AZ ZUCKERMAN (London, England). *Br Med J* 1988;297:86-8.

**Failure of a human immunodeficiency virus (HIV) immune globulin to protect chimpanzees against experimental challenge with HIV**  
AM PRINCE, B HOROWITZ, L BAKER, *et al* (New York, USA). *Proc Natl Acad Sci USA* 1988;85:6944-8.

**Human immunodeficiency virus type 1 challenge of chimpanzees immunised with recombinant envelope glycoprotein gp 120**  
PW BERMAN, JE GROOPMAN, T GREGORY, *et al* (San Francisco, USA). *Proc Natl Acad Sci USA* 1988;85:5200-4.

**Other sexually transmitted diseases**

**Chancroid: clinical variants and other findings from an epidemic in Dallas county 1986-1987**  
ME MCCARLEY, PD CRUZ, RD SONTHEIMER (Dallas, USA). *J Am Acad Dermatol* 1988;19:330-44.

**Reappearance of hepatitis B virus in immune patients infected with the human immunodeficiency virus type 1**  
Y LAZIZI, L GRANGEOT-KEROS, JF DELFRAISSY, *et al* (Clamart, France). *J Infect Dis* 1988;158:666-7.

**Antibody to human immunodeficiency virus (HIV) and sub optimal response to hepatitis B vaccination**  
AC COLLIER, L COREY, VL MURPHY, HH HANDSFIELD (Seattle, USA). *Ann Intern Med* 1988;109:101-5.

**Prednisone withdrawal followed by recombinant alpha interferon in the treatment of chronic type B hepatitis: a randomized, controlled trial**  
RP PERILLO, FG REGENSTEIN, MG PETERS, *et al* (St Louis, USA). *Ann Intern Med* 1988;109:95-100.

**Cytomegalovirus infection and treatment with ganciclovir**  
*Rev Infect Dis* 1988;10suppl:457-563.

**Outcome of untreated *Entamoeba histolytica* in homosexual men with and without HIV antibody**  
E ALLASON-JONES, A MINDEL, P SARGEANT, D KATZ (London, England). *Br Med J* 1988;297:654-6.

**Genitourinary bacteriology****The association of *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and group B streptococci with preterm rupture of the membranes and pregnancy outcome**

LS ALGER, JC LOVCHIK, JR HEBEL, LR BLACKMON, MC CRENSHAW (Baltimore, USA). *Am J Obstet Gynecol* 1988;159:397-403.

Several observations support the hypothesis that maternal genital infections play a causal role in preterm delivery. The authors investigated the prevalence of endocervical infection with *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and group B streptococci in patients with premature rupture of membranes (PRM), compared with a control group from the same obstetric population. Fifty two women entering the labour and delivery suite of the University of Maryland Hospital from January 1983 to March 1984 with spontaneous rupture of membrane preceding the onset of contractions at 20 to 37 completed weeks of gestation were admitted to the study. Patients who had uterine anomalies, diabetes mellitus, or had received antibiotics within four weeks of presentation were excluded. Eighty four patients attending antenatal clinics were selected as controls.

Microbiological specimens were obtained sequentially from the endocervical canal for culture of *N gonorrhoeae*, group B streptococci, and *C trachomatis* on presentation with PRM. Identical endocervical specimens were taken from control patients receiving antenatal care at the same gestational age as the matched patient. Patients with PRM and controls had been screened for infection with *N gonorrhoeae* at their initial antenatal visit, and those with positive cultures had been treated with intramuscular penicillin. Neither group of patients had been screened or treated for group B streptococci or *C trachomatis* before study cultures were obtained. In the absence of any clinical signs of infection, patients with PRM at 26 to 36 weeks of gestation were routinely given betamethasone and, if indicated by the presence of contractions, tocolytic agents in an attempt to delay delivery and promote fetal lung maturation. Patients were not given antibiotic treated for *C trachomatis* infection until after delivery. *C trachomatis* was isolated from 23/52 (44%) patients with PRM versus 13/84 (15%) women in the control group. Group B streptococci were isolated from 7/45 (16%) of the patients with PRM versus 3/80 (4%) controls. *N gonorrhoeae* was isolated from 6/52 patients with PRM versus 0/84 controls, although three

controls had been infected with *N gonorrhoeae* earlier in pregnancy. Infection with more than one pathogen was found in four patients with PRM but in none of the controls. Of the 48 patients with PRM who were screened for all three organisms, only 16/48 (33%) were uninfected, compared with 68/84 (81%) of the control group.

In this study the increased risk of PRM associated with *C trachomatis* infection was significant ( $p < 0.001$ ) with and without adjustment for other potential risk factors. This was also true for group B streptococcal infection ( $p = 0.002$ ). The risks of PRM associated with *C trachomatis* and group B streptococci were found to be mutually independent. Endocervical infection did not significantly affect the incidence of early maternal or neonatal complications after delivery other than resulting in chlamydial or gonococcal conjunctivitis, or clinical presentation compatible with early onset group B streptococcal pneumonitis in those at risk.

K Shanmugaratnam

#### Isolation of genital mycoplasmas and *Chlamydia trachomatis* in stillborn and neonatal autopsy material

E MADAN, MP MEYER, A AMORTEGUI (Huntington, USA). *Arch Pathol Lab Med* 1988;112:749-51.

### Public health and social aspects

#### A clinical trial of nonoxynol-9 for preventing gonococcal and chlamydial infections

WC LOUV, H AUSTIN, WJ ALEXANDER, S STAGNO, J CHEEKS (Cincinnati, USA). *J Infect Dis* 1988;158:518-23.

### Miscellaneous

#### Effect of cigarette smoking on cervical epithelial immunity: a mechanism for neoplastic change?

SE BARTON, PH MADDOX, D JENKINS, R EDWARDS, J CUZICK, A SINGER (London, England). *Lancet* 1988;ii:652-4.

#### Risk of cervical cancer associated with mild dyskaryosis

JH ROBERTSON, BE WOODEND, EH CROZIER, J HUTCHINSON (Belfast, Northern Ireland). *Br Med J* 1988;297:18-20.

#### Colposcopy in teenagers

NG HADDAD, IY HUSSEIN, JRB LIVINGSTONE, GE SMART (Edinburgh, Scotland). *Br Med J* 1988;297:29-30.

#### Changing nature of anal cancer

RW TALBOT (London, England). *Br Med J* 1988;297:239-40.

#### Neonatal meningitis due to *Gardnerella vaginalis*

L BERARDI-GRASSIAS, O ROY, JC BERARDI, J FURIOLI (Mantes La Jolie, France). *Eur J Clin Microbiol Infect Dis* 1988;7:406-7.

#### Association of *Ureaplasma urealyticum* infection of the lower respiratory tract with chronic lung disease and death in very-low-birth-weight babies

GH CASSEL, KB WAITES, DT CRUISE, *et al* (Birmingham, USA). *Lancet* 1988;ii:240-4.

#### Recurrent vaginitis as a result of sexual transmission of IgE antibodies

SS WITKINS, J JEREMIAS, WJ LEDGER (New York, USA). *Am J Obstet Gynecol* 1988;159:32-5.

#### Gonococcal and chlamydial antibodies in ectopic and intrauterine pregnancy

JN ROBERTSON, P HOGSTON, ME WARD (Southampton, England). *Br J Obstet Gynaecol* 1988;95:711-6.

#### CD8 cell responses to herpes simplex virus in Behcet's disease

C YOUNG, T LEHNER, CG BARNES (London, England). *Clin Exp Immunol* 1988;73:6-10.

#### Lichen sclerosis et atrophicus

B GARCIA-RAVO, P SANCHEZ-PEDREÑO, A RODRIGUEZ-PICHARDO, F CAMACHO (Seville, Spain). *J Am Acad Dermatol* 1988;19:482-5.

#### Empirical therapy for the management of acute proctitis in homosexual men

AM ROMPALO, P ROBERTS, K JOHNSON, WE STAMM (Seattle, USA). *JAMA* 1988;260:348-53.

Rampalo *et al* propose that an effective empirical treatment regimen would provide a rapid and less expensive approach to the management of homosexual men presenting with acute proctitis. They evaluated 129 men with symptoms suggestive of acute proctitis, and after some had been excluded for appropriate criteria (including a clinical diagnosis of herpes simplex virus (HSV) infection or primary syphilis), 87 men were randomised to two groups. Thirty nine men

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(group E) received treatment with 4.8 MIU aqueous penicillin G procaine and 1 g oral probenecid, followed by 100 mg of oral doxycycline twice a day for seven days. The other 48 men (group S) were given specific treatment for each infection as it was recognised. The two groups were well matched, and initial evaluation included examination for evidence of proctitis and comprehensive microbiological screening.

The pathogens found most commonly were HSV (in 29%), *Neisseria gonorrhoeae* (16%), and *Chlamydia trachomatis* (15%); and no pathogen was identified in 28% of patients. There were three follow up visits at weekly intervals, when symptoms, signs, and microbiological cure were assessed, and for all three variables group E were shown to have responded more quickly. The difference in response between the two groups was less pronounced, however, by the third week. Several of the original 87 patients did not attend for all follow up visits.

Interpretation of the results was made difficult because, whereas patients in group E received treatment at the initial visit, most in group S were not treated until the first follow up visit, when a pathogen had been identified. It is therefore not unexpected that most patients in group S still had symptoms or signs of proctitis compared with those who had already been treated. The study was designed to exclude HSV proctitis on clinical examination, but 25 of 41 patients with HSV infection were randomised, forming 29% of the study population who would be expected to be "non-responders".

The authors recommend that homosexual men presenting with acute proctitis should undergo full clinical and microbiological examination, and patients in whom herpes, gonorrhoea, or syphilis is diagnosed should be treated specifically. If no diagnosis is made at the initial consultation, empirical treatment as detailed above should be initiated. The principle of early treatment for quicker resolution of symptoms is indisputable. Although not suggested by the authors, it might be worth considering the addition of acyclovir to the above regimen in view of the high incidence of HSV infection, although this would, of course, increase the cost of treatment.

C Thompson

#### The Wellcome international antiviral symposium

*Am J Med* 1988;85:suppl:1-212.